

Remarks/Arguments

The foregoing amendments are of formal nature and are fully supported by the specification as originally filed.

Claims 58, 59, 61-66 and 81-87 are pending in this application. Claims 62-64 and 66 have been withdrawn from consideration; claims 58, 59, 61, 65 and 81-87 stand rejected on various grounds. All rejections are respectfully traversed. With the current amendment, claims 58, 61, 82, 86 and 87 are amended, and new claims 88-96 are added. The amendments are of formal nature, and new claims 88-96 have been added on the analogy of pending claims 59-66, and 84-85. The amendments to do add new matter.

Withdrawn Objections/Rejections

Applicants appreciate the withdrawal of all prior objections and rejections in view of Applicants' amendments and/or arguments.

New Rejections

*Objections to the Claims*

Claim 87 has been objected to for its dependence on claim 96, which does not exist. The foregoing amendment, which corrects this typographical error, should overcome the present objection.

*Claim Rejections - 35 U.S.C. 112, second paragraph*

Claims 58-59, 61, 65 and 81-87 were rejected as "indefinite."

A. Claim 58 and all dependent claims were rejected for allegedly failing to provide sufficient antecedent basis for the recitation of "the compound," "said conjugate," and "said compound" in Claim 58. Although Applicants believe that Claim 58, as rejected, complied with the requirement of antecedent basis for all terms concerned, the claim has been amended to specifically recite non-oligomeric organic compounds and target protein-compound conjugates

at all occurrences. Accordingly, the present rejection should be withdrawn.

B. Claims 59 and 61, and all dependent claims, were rejected for their recitation of "the ligand," which, in the Examiner's view, did not have sufficient antecedent basis. Although Applicants believe that it was proper to refer to "the ligand" in view of the recitation of a "novel ligand" in claim 58, claims 59 and 61 have been rejected to specifically refer to the "novel" ligand, which should overcome their rejection.

C. Claim 82 was rejected for its recitation of the term "associated" with a cysteine, which was held to be "vague and indefinite." The current amendment of claim 82, which clearly states that the -SH group in part of the cysteine, is believed to overcome this rejection.

D. Claims 83-85 were rejected for their recitation of "the library." Claims 83-85 depend on claim 58, which, in step (a) provides a clear antecedent basis for "library." Accordingly, the present rejection is submitted to be in error, and should be withdrawn.

E. Claim 87 was rejected for its reference to "the compound." The current amendment of Claim 87, which replaces the phrase "the compound" by "the non-oligomeric organic compound" is believed to overcome its rejection.

#### ***Claim Rejections - 35 USC § 103***

Claims 58-59, 61, 65, and 81-87 (all claims under examination) have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Kim et al. (WO 98/11436, March 19, 1998) and Siuzdak, G. (Mass Spectrometry for Biotechnology, New York: Academic Press, 1996, pages 119-126).

Kim et al. describes a method of detecting a ligand that binds to a target molecule. The ligand and the target molecule each contains, as obtained or modified, a member of a binding pair, to permit covalent linkage or tethering of the ligand when bound to the target molecule. In one embodiment, the binding pair consists of sulfhydryl groups. According to the rejection, the only difference between the claimed invention and Kim et al. is the use of mass spectrometry. The Examiner cited Siuzdak for its teaching of electrospray mass spectrometry, which is said to have "demonstrated its potential in the analysis of non-covalent interactions between an antibody

and a hapten, and for observing covalent protein-bound intermediates in an antibody-catalyzed reaction." The quoted statement, in the Examiner's reading, "would encompass the 'antibody-antigen' complexes disclosed by Kim et al." The Examiner adds that there would have been a motivation to combine the teaching of Kim et al. with Siuzdak, since "Siuzdak explicitly states that electrospray has 'demonstrated its potential' for these systems."

Applicants disagree and respectfully traverse the rejection.

The use of mass spectrometry is not the only difference between the invention claimed in the present application and the disclosure of Kim et al. Part (c) of claim 58 and claim 86 specifies that mass spectrometry is used to detect the "most abundant target protein-compound conjugate that is formed." Claim 58 additionally states that the identity of the non-oligomeric organic compound present in the most abundant target protein-compound conjugate is identified "as the non-oligomeric organic compound having the greatest relative affinity for the target protein." Finally, claim 87, which depends on claim 86, recited the determination of the identity of the non-oligomeric organic compound that is disulfide bonded to the target protein in the most abundant target protein-compound conjugate that is formed.

The Examiner's analysis of Kim et al. does not account for these recitations. Indeed, Kim et al. does not disclose these elements of claim 58, claim 86, or claim 87. Since Siuzdak does not make up for these deficiencies of Kim et al., the combination of Kim et al. and Siuzdak et al. does not make obvious the invention claimed in the rejected claims.

Furthermore, Siuzdak does not explicitly state that electrospray mass spectrometry has demonstrated its potential for identifying ligands present in a covalent conjugate between a target protein and a ligand of the protein. The quoted brief sentence is limited to the observation of covalent-bound intermediates in an antibody-catalyzed reaction. Observing a chemical entity, such as a protein-bound intermediate, and determining the identity of such chemical entity are two very different things. Accordingly, Siuzdak et al. does not provide the motivation relied upon by the Examiner for making the combination relied upon in the present rejection.

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39750-0002DV1).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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